Reply to "Antiviral and anti-inflammatory properties of ivermectinand its potential use in Covid-19"☆

En respuesta a "Propiedades antivirales y antiinflamatorias de ivermectina y su potencial uso en COVID-19"

To the Editor:

In their letter regarding our review entitled "Antiviral and anti-inflammatory properties of ivermectin and its potential use in Covid-19", the authors call upon "...professionals to practice responsible science..." with regard to "...the recommendation of treatments with ambiguous risk-benefit profiles". In the last paragraph of our review we stated that "evidence suggests that this drug can act at different stages of the disease" but that "controlled studies must be conducted first to demonstrate the effect of ivermectin against Covid-19."[1]

Our article was submitted to Archivos de Bronconeumología on June 9 of this year and accepted by the editors after peer review on June 15 without any correction. All the articles available on the subject were included. Those responsible for editing the final version modified the reference of Patel et al. to "N Engl J Med. 2020, https://doi.org/10.1056/NEJMoa2001282.5", cited by us as "Patel AN, Desai SS, Grainger DW, Mehra MR. (2020). Usefulness of ivermectin in COVID-19 illness. Published April 19, 2020 (preprint) (Patel et al., 2020) doi: 10.1056/NEJMoa2001282.5". We were unaware of this change until we began to draft this reply. When we access the referenced doi, the article does not appear, and when we questioned the editors of the NEJM, they replied that they could not confirm or deny anything that had not been published, as the process is confidential. When we submitted our manuscript, we did not know that reference 3 would be removed without a trace. The authors of the letter to which we reply refer to the article "Ivermectin in COVID-19 related critical illness", withdrawn from the ssm.com repository,[2] as if it were the one we cited. Both studies use data extracted from material collected by Surgisphere Corporation, whose founder is Sapan Desai, co-author. Dr Desai, along with A. Patel, M. Mehra and F. Ruschitzka published in The Lancet a paper entitled "Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis" in which they reported that these drugs increased mortality rates. This prompted multiple criticisms of the egregious methodological flaws that culminated in the last 3 authors submitting a comment to the magazine, published on June 5.[3] in which they retracted their article because of serious concerns about the veracity of the data with which they had worked. That same day, The Lancet withdrew the article.[4] On 25 June, the NEJM did the same with "Cardiovascular disease, drug therapy, and mortality in Covid-19."[5]

The corresponding author of our paper is a member of the Covid-19 Expert Committee. This guarantees the autonomy of his actions, as the Peruvian Ministry of Health, like all scientific societies and state health agencies the world over, selects doctors that have no conflicts of interest in the matter in which they are consulted.

A few months after the pandemic began, 34 clinical trials were registered, 2 of which are already completed, and these will help determine if ivermectin is useful in the treatment and prophylaxis of Covid-19. In a few more months we hope to have the answer.

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The Importance of Dependence in Global Assessment of Hospitalized Patient☆

La importancia de la dependencia en la valoración global del paciente hospitalizado

To the Editor:

We read with great interest the article by Fernández-García et al.[1] recently published in Archivos de Bronconeumología on the assessment of dependence as a predictor of mortality following hospitalization for COPD exacerbations. The authors developed 3 scores for predicting mortality that included the variables age > 60 years, FEV1 < 50%, and Charlson Index (CI) ≥ 3. They were surprised to find that dependence, measured by the Barthel and Lawton and Brody indices are independent predictors of mortality that carry a greater weight than other conventional variables.

Despite the existence of different dependency scales[2], few publications in the scientific literature allow us to correctly evaluate their weight in the morbidity and mortality of our patients[3,4]. Our group recently reported data from a cohort of 305 octogenarians with multiple diseases and a prevalence of COPD of 21.3%, in which

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different scales, including the OARS (*Older Americans Resources and Services*) questionnaire, were used to evaluate dependence in both basic activities of daily living (BADL) and instrumental activities of daily living (IADL)[5]. Using the age-adjusted Charlson index, 83.3% of our patients had a predicted 1-year mortality rate of 85%, compared with a real mortality rate of 57.7% at 18 months. We too were surprised by the power of dependence in terms of mortality prediction, and that the degree of dependence in the subgroup with a predicted 1-year mortality rate of 85% was higher for both BADL (6.6 ± 5 vs. 4.1 ± 4; $p = 0.001$) and IADL (9.7 ± 4.6 vs. 6.7 ± 4.8; $p < 0.001$).

Multiple factors influence the overall mortality of our patients. Dependence is a factor that can predict mortality more reliably than other conventional indices such as the Charlson Index. As we mentioned above, this index overestimates the risk of 1-year mortality and proves ineffective, while the assessment of dependence adds more weight to the prediction of short-term mortality. In a healthcare setting in which demand is progressively increasing, we need better tools to predict mortality and to help us use resources rationally based on the benefit we can provide to our patients.

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Conflict of interests

The authors state that they have no conflict of interests.

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Reply to "*The Importance of Dependence in Global Assessment of Hospitalized Patient*"☆

Respuesta a La importancia de la dependencia en la valoración global del paciente hospitalizado

To the Editor:

We have read with interest the letter published regarding our article entitled *The Importance of Dependence in the Global Assessment of Hospitalized Patients*.[1,2] We thank the authors for their comments on our research and agree with the main message of their letter, as it serves to reinforce the importance of dependence in performing activities (both basic and instrumental) in the prediction of mortality in patients with chronic diseases. We have observed that, independently or in addition to the many other clinical, demographic, or functional variables usually included in the scores used in clinical practice, variables related to dependence improve these scores and provide prognostic information.[1–3]

We would like to make a couple of comments on this communication. First, Briongos-Figuero et al.[1] comment on our surprise that dependence for performing activities was an independent factor for mortality, with a higher capacity for prediction than other clinical variables in patients admitted for COPD exacerbation. However, in the introduction to the article we said that what surprised us was the scant evidence available in this field in COPD, unlike in other chronic diseases, since the results of our study were far from a surprise. In the SocioCOPD cohort itself, on which we carried out the mortality study, dependence for performing basic activities determined by non-specific COPD indices, such as Barthel, not only influences this event, but is also one of the variables that best predicts short- and long-term readmissions for any cause after a severe exacerbation of COPD[4]. Indeed, this is one of the alternative hypotheses of the initial research project. What surprised us, and still does, is that so little emphasis is placed on this area in the clinical practice guidelines on COPD.

Secondly, the authors refer to an interesting study that they published recently, and point out the limited value of comorbidities (determined by the Charlson index) when adjusted for disability in the prediction of mortality,[3] an outcome that differs from our findings. In all the predictive models explored in the SocioCOPD cohort, the number of comorbidities measured by this index did have a predictive capacity, although the power was less than for dependence for both basic and instrumental activities.[2] However, we would like to emphasize that these 2 studies are not at all comparable, as the mean upper age of our correspondents' series was almost 20 years older than ours, they had many more comorbidities, and, in particular, less than 20% of their patients were identified as having "chronic respiratory disease".[3] In a large COPD population[5] with a high comorbidity burden and age closer to that included in the study of Briongos-Figuero et al.,[3] reported by a working group of the Spanish Society of Internal Medicine, the 2 factors that carried the greatest weight for predicting mortality were comorbidity and disability.

Therefore, we also believe that it is important to continue research in this line, as it does not appear to be exclusive to elderly patients with multiple diseases, but also affects to a large extent younger subjects with specific predominant diseases, such as COPD in this case.

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